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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/666,022	09/17/2003	Dennis M. Klinman	4239-66899	7954

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Klarquist Sparkman, LLP
One World Trade Center, Suite 1600
121 S.W. Salmon Street
Portland, OR 97204

EXAMINER	
HORNING, MICHELLE S	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
04/02/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/666,022	KLINMAN ET AL.	
	Examiner	Art Unit	
	MICHELLE HORNING	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-6,8-22 and 25-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4-6, 8-22, 25-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is responsive to communication filed 1/2/2009. Any rejection not reiterated has been withdrawn.

Response to Amendment

The declaration under 37 CFR 1.132 filed 6/5/2008 is insufficient to overcome the rejection of claims 1, 2, 4-6 and 9-34 based upon 35 USC 102(e) and 35 USC 103 as set forth in the last Office action because: the declaration by Dr. Verthelyi is not found persuasive for showing that one of ordinary skill in the art could not predict the effectiveness of the claimed methods based on the cited prior art. This is not found persuasive because, firstly, the data provided is not commensurate in scope with the instant claims, as the claims are generally drawn to any immunocompromised patient and treatment of any secondary infection, (e.g., even whether having been diagnosed or not). However, the data provided in the declaration is limited to a very specific experiment that analyzed limited immune parameters and there are other facets of treatment that have not been shown that are unpredictable. For example, by treating immunocompromised patients in the prior art, one would inherently provide treatment to any opportunistic secondary infections, as an increase in the immune system by treatment of viruses, cancers, etc. as taught by Klinman would provide treatment for secondary infections. Treatment of secondary infections is multi-faceted, as such infections can be treated by direct or indirect mechanisms. For instance, a secondary infection in an immunodeficient patient would effectively be treated by treating the cause of the immunodeficiency, which

would boost the immune system, thus treating the secondary infection via an increase in the immune system, or the infection could be treated directly from the treatment. Also, obviousness does not require absolute predictability. The data provided appears to be limited showing attempting to rebut absolute predictability.

The declaration also fails to provide a showing of unexpected results because there is no direct comparison with the closest prior art. However, it is noted that a direct comparison with the closest prior art may not be possible in this instance, since the prior art discloses basically all of the same method steps recited in the instant claims, e.g., administration of the D ODN in an immunocompromised patient. The presence of a secondary infection is inherent to the patient population of immunocompromised patients in the prior art, as such patients develop "secondary infections" due to being immunocompromised. The step of "evaluating the immune response" is broad and encompasses merely a mental step (e.g., feeling better, noticing lesions diminishing, etc.). There are no actual active steps recited for such "evaluating the immune response" that would differentiate this broad limitation over the cited art, other than in new claim 34. Note, the steps which include only a mental process may not further limit a method claim. Further, the showing is not commensurate in scope with the instant claims, as the claims are drawn to any immunocompromised patients (which would include organ transplant recipients, etc.) having any possible secondary infection. The data provided only shows that the D ODN was effective for SIV infected macaques for certain lesions, while those treated with K ODN

were not as effective for treating such lesions. However, Klinman discloses the use of D ODN and not K ODN, thus, there is no direct comparison with the closest prior art.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 8-17 and 21 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent No. 6977245 (hereinafter as "Klinman et al"). The Office apologizes for mistakenly applying a 35 USC 102(b) rejection. This is corrected to a 35 USC 102(e). Any inconvenience is regretted.

Klinman discloses the use of "D type CpG oligodeoxynucleotides" and a method of using these ODNs to induce an immune response (see Abstract). Further, the sequences set forth by SEQ ID NO: 177 and SEQ ID NO: 1 of the instant application is taught by SEQ ID NO: 1 of this prior art reference. These sequences include phosphodiester bases in both the CpG motif and its immediate flanking regions (see paragraph 94 and Table 1). Also see Table 1, for self-complementary sequences in bold. Infectious agents include viruses,

bacteria and fungi (see paragraph 48) as well as Leishmania and hepatitis (see paragraph 135). Paragraph 129 describes administration of the ODN either alone or in combination with another molecule. While this reference does not describe any secondary infections, this reference meets the claims in administering the oligo to immunocompromised subjects *prior to* exposure to the secondary infection. With respect to an immunocompromised subject, the authors provide the following in paragraph 47: A disease or disorder in which the subject's immune system is not functioning in normal capacity or in which it would be useful to boost a subject's immune response. Immune system deficiencies include those diseases or disorders in which the immune system is not functioning at normal capacity, or in which it would be useful to boost the immune system response. In one specific, non-limiting example, a subject with an immune system deficiency has a tumor or cancer (e.g. tumors of the brain, lung (e.g. small cell and non-small cell), ovary, breast, prostate, colon, as well as other carcinomas and sarcomas). Thus, Klinman meet the limitations of the rejected claims above.

Response to Arguments

Applicant's arguments filed 1/2/2009 have been fully considered but they are not persuasive. Applicant asserts that Klinman fails to disclose agents for the use of immunocompromised subjects let alone to treat secondary infections. This

is not found persuasive. Klinman discloses broad patients having an immune system deficiency which is clearly an immunocompromised subject. Klinman teaches this for a wide variety of infections, including viruses etc and those having an immune deficiency which is a patient population which is inherently subjected to secondary infections due to a weaken immune system. Note that the secondary infections as recited in the claims include any type of secondary infection whether diagnosed or not. Since such infection causing germs are ubiquitous, any patient having an immune system deficiency would be expected to have some type of secondary infection given its broadest reasonable interpretation. Applicant also asserts that Klinman does not disclose an evaluation of an immune response to a secondary infection. This is not persuasive as a step of evaluating is broad and encompasses merely mental steps, such as feeling better, observing a lesion decreasing in size, etc. There are not active steps in the claims (except new claim 34) that limit the evaluation step to differentiate it over the prior art. A mental step does not usually provide patentability. However, as discussed below, Klinman teaches determining Ab titer as a means for determining effectiveness, showing that this is well known in the art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which

said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 4-6, 9-22 and 25-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over combined teachings of Klinman et al (see above) and Fraternale et al (2000).

The teachings of Klinman et al fail to describe the following: the co-administration of HAART or AZT with an ODN for immunocompromised subjects. Note that Klinman does describe using his claimed oligos for immune system deficiencies which would include HIV or AIDS (human immunodeficiency virus or autoimmune disease syndrome). As discussed above, it would be useful to boost a subject's immune system with either HIV or AIDS particularly given potential exposure to secondary infections and this would be obvious to the ordinary artisan. Also note that the teachings of Klinman et al characterize the responses to the oligos in all of the figures, including their activation of NK cells and PBMCs. It would have been obvious to one of ordinary skill in the art to

potentiate an immune response by methods and oligos successfully described in the prior art for subjects with an immune deficiency and then evaluate the results to determine the success rate, particularly in immune deficient subjects exposed to some secondary infection. To address new claims 33-34, Klinman discloses determining antibody titer as a mean of evaluating the effectness of the treatments disclosed therein; see the description of Figure 6 in the specification. It is noted since Klinman discloses patients having various conditions, including viral infections and various immunocompromised conditions, the ordinary artisan would extrapolate this teaching in order to determine the antibody titer for measuring the effectiveness for various conditions as this is very well known in the art.

Fraternale et al discuss the use of combination antiretroviral therapy in patients with HIV-1, including protease and reverse transcriptase inhibitors (see Abstract). This reference discloses that AZT is known for its anti-HIV-1 activity and has been shown to reduce progression of AIDS. Also, this reference teaches that HAART produces a decline in plasma virus to undetectable levels in many patients (see Discussion). Thus, it would have been obvious to one of ordinary skill in the art to combine either HAART or AZT with an ODN to further stimulate an immune response in a subject infected with HIV. One would have been motivated to do so, as suggest by Fraternale et al, because "patients entering these treatments are usually at advanced stages of the disease and have a poor immunologic status" (see page 219). There would have been a reasonable expectation of success given that the success of an ODN in eliciting immune

responses against HIV is known as well as the success rate of both HAART and AZT in combating HIV. The invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicant's arguments filed 1/2/2009 have been fully considered but they are not persuasive. Applicant's arguments directed to Klinman have been discussed above. Applicant asserts that Fraternale does not describe the effect of any therapeutic effect on secondary infections. In response, such an effect need not to be disclosed in the prior art as this is a property of its administration and not an active step in the claim.

Conclusion

NO CLAIM IS ALLOWED.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will

the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELLE HORNING whose telephone number is (571)272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michelle Horning/
Examiner, Art Unit 1648

/Eileen B. O'Hara/
Supervisory Patent Examiner
Art Unit 1644